ABSTRACT

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Title of Diploma Thesis: The development of method for the determination of atorvastatin and its impurities in tablets using supercritical fluid chromatography

This diploma thesis was focused on developement and optimization of a method for qualitative and quantitative evaluation of atorvastatin and its impurities using supercritical fluid chromatography. One of the main goals was to optimize chromatographic conditions, which included the selection of a sufficiently selective stationary phase, appropriate modifier and mobile phase additives. Effect of pressure was also explored. Finally this method was validated.

A total of seven analytes were evaluated, lately only six of them. One impurity was impossible to separate without using a chiral stacionary phase since it was an enantiomer of atorvastatin. Measurements were performed on UPC^2 Acquity system with PDA detector by Waters. Selected wavelength for detection was 245 nm.

Tested stationary phases included columns dedicated for SFC, namely Acquity UPC^2 BEH 1,7 µm, BEH 2-EP 1,7 µm, HSS C18 SB 1,8 µm a CSH Fluoro-Phenyl 1,7 µm (all of them 3,0 x 100 mm). Insufficient separation using these columns resulted in testing columns used in HPLC. Best results were provided by Ascentis Express F5 2,7 µm (3,0 x 100 mm).

Mobile phase for gradient elution consisted of pure CO_2 with organic modifier methanol and additives ammonium formate (15 mM), formic acid (1 %) and water (5 %). The gradient was set to change from 2 % to 30 % of modifier with additives within 3 minutes. Flow rate of mobile phase was 2.5 ml / min. The column was thermostated at 40 ^{o}C, pressure on ABPR was set at 2000 psi. The method was applied to samples of tablets past expiry date and tablets used for stability studies.